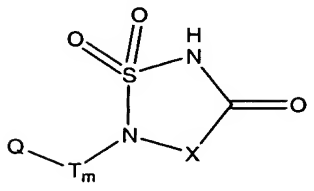
Claims:

1. A compound of formula (**I**):



(**I**)

or a pharmaceutically acceptable salt thereof, wherein:

Q is an optionally substituted group selected from C_{1-8} aliphatic, C_{6-10} aryl, heteroaryl having 5-10 ring atoms, and heterocyclyl having 3-10 ring atoms;

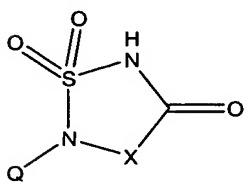
T is selected from a C_{1-6} alkylidene chain wherein one or two non-adjacent methylene units of T are optionally and independently replaced by -O-, -NR-, -S-, -C(O)-, -C(O)NR-, -NRC(O)-, -NRC(O)NR-, -SO-, $-SO_2-$, $-NRSO_2-$, $-SO_2NR-$, or $-NRSO_2NR-$;

m is selected from zero or one;

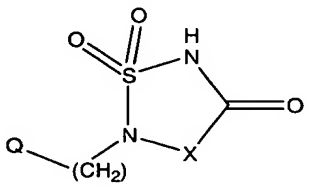
X is selected from $-CH_2-$, -C(O)-, or $-CF_2-$; and

each R is independently selected from hydrogen or an optionally substituted C_{1-8} aliphatic group, or two R groups bound to the same nitrogen are taken together with the nitrogen to form a 3-7 membered heterocyclic ring having 0-2 heteroatoms in addition to the nitrogen, wherein said heteroatoms are independently selected from nitrogen, oxygen, or sulfur.

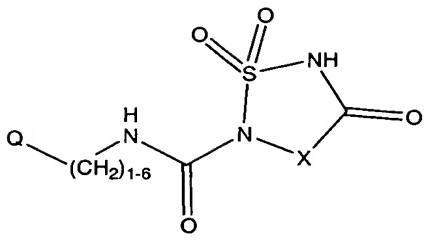
2. The compound according to claim 1 wherein said compound is selected from:



(**I-A**),



(**I-B**),



or (**I-C**);

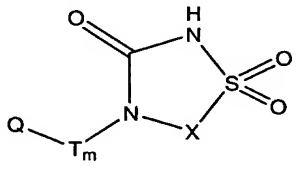
or a pharmaceutically acceptable salt thereof.

3. The compound according to claim 2 wherein Q is selected from C_{6-10} aryl and 5-6 membered heterocyclyl.

4. The compound according to claim 2 wherein X is $-CH_2-$.

5. The compound according to claim 1 wherein said compound is selected from a compound depicted in Table 1.

6. A compound of formula (**II**):



(**II**)

or a pharmaceutically acceptable salt thereof, wherein:

Q is an optionally substituted group selected from C_{1-8} aliphatic, C_{6-10} aryl, heteroaryl having 5-10 ring atoms, and heterocyclyl having 3-10 ring atoms;

T is selected from a C_{1-6} alkylidene chain wherein one or two non-adjacent methylene units of T are optionally and independently replaced by -O-, -NR-, -S-, -C(O)-, -C(O)NR-, -NRC(O)-, -NRC(O)NR-, -SO-, $-SO_2-$, $-NRSO_2-$, $-SO_2NR-$, or $-NRSO_2NR-$;

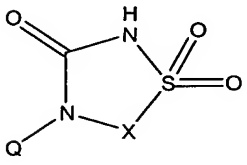
m is selected from zero or one;

X is selected from $-CH_2-$, -C(O)-, or $-CF_2-$; and

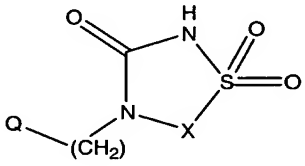
each R is independently selected from hydrogen

or an optionally substituted C_{1-8} aliphatic group, or two R groups bound to the same nitrogen are taken together with the nitrogen to form a 3-7 membered heterocyclic ring having 0-2 heteroatoms in addition to the nitrogen, wherein said heteroatoms are independently selected from nitrogen, oxygen, or sulfur.

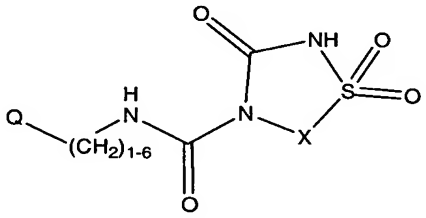
7. The compound according to claim 6 wherein said compound is selected from:



(II-A),



(II-B),



or **(II-C)**;

or a pharmaceutically acceptable salt thereof.

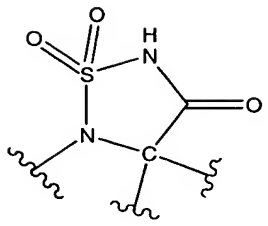
8. The compound according to claim 7 wherein Q is selected from C_{6-10} aryl and 5-6 membered heterocyclyl.

9. The compound according to claim 7 wherein X is $-CH_2-$.

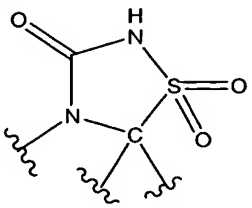
10. A pharmaceutical composition comprising a compound according to any one of claims 1-9 and a pharmaceutically acceptable carrier, adjuvant, or vehicle.

11. The composition according to claim 10 wherein the composition comprises an additional therapeutic agent.

12. A phosphate isostere having the formula:



(I-D) or



(II-D).

13. The phosphate isostere of claim 12 wherein said phosphate isostere is a phosphate bioisostere.

14. A protein:ligand complex wherein the ligand is a compound according to any one of claims 1-9.

15. The complex according to claim 14 wherein said protein is an enzyme.

16. The complex according to claim 15 wherein said enzyme is a binding domain for the ligand.

17. The complex according to claim 16 wherein said binding domain is a receptor for the ligand.

18. The complex according to claim 17 wherein said receptor comprises a binding pocket.

19. The complex according to claim 14 wherein said compound is a substrate of the protein.

20. The complex according to claim 14 wherein said compound is an inhibitor of the protein.

21. The complex according to claim 14 wherein said compound is an agonist of the protein.

22. The complex according to claim 14 wherein said compound is an antagonist of the protein.

23. The complex according to claim 14 wherein said protein is a phosphatase.

24. The complex according to claim 23 wherein said phosphatase is SHP-2.

25. A method for using a compound comprising a sulfhydantoin moiety or a reverse sulfhydantoin moiety as a phosphate isostere comprising the step of contacting said compound with a protein, wherein a natural ligand of said protein comprises at least one mechanistically significant phosphate group.

26. The method according to claim 25 wherein said protein is an enzyme.

27. The method according to claim 26 wherein said enzyme is a binding domain for the natural ligand.

28. The method according to claim 27 wherein said binding domain is a receptor for the natural ligand.

29. The method according to claim 28 wherein said receptor comprises a binding pocket.

30. The method according to claim 25 wherein said natural ligand is a substrate of the protein.

31. The method according to claim 25 wherein said natural ligand is a second protein.

32. The method according to claim 25 wherein said natural ligand is an agonist of the protein.

33. The method according to claim 25 wherein said natural ligand is an antagonist of the protein.

34. The method according to claim 25 wherein said compound is used as a phosphate bioisostere.

35. The method according to claim 25 wherein said protein is selected from the group consisting of phosphatase; kinase; nucleotidase; SH2; dehydrogenases, oxidase, reductases and other NAD-dependent proteins or flavin-dependent proteins; RNA and DNA helicases; RNA and DNA polymerases; sodium/potassium ATPase (proton pump); P-type cation transport ATPases; carboxykinase; ATP synthase; ATP-dependent proteases; phosphotransferases; phosphoribosyltransferase; myosins, kinesins, and other motor proteins; dynamins and dynamin-like proteins; ADP-ribosylation factors; DNA repair proteins; RNA splicing proteins; DNA ligases; coenzyme A-dependent enzymes; acyl carrier protein phosphopantetheine domains; citrate lyases; thiamine pyrophosphate-dependent proteins; phosphodiesterases; RNA cyclases; carbamoyl-phosphate synthases; glucosamine-6-phosphate isomerase; triosephosphate isomerase; ribulose-phosphate 3-epimerase; pyridoxal-phosphate-dependent proteins; cAMP- and cGMP-dependent proteins; PID (phosphotyrosine-interacting domain) proteins; phospholipases; phosphatidylethanolamine-binding protein; PH domains; phospholipid-binding proteins; phosphate-dependent receptors; inositol phosphate-binding proteins; phosphotyrosine-binding proteins; phosphoserine-binding proteins; phosphohistidine-binding proteins; phosphate-dependent transcriptional regulators; phosphate-dependent transporters; sulfate-dependent transporters; NTPases; DNA replication proteins; nucleotide-sugar transferases; phosphorylases; sugar phosphotransferases; sulfatases; nucleases; and arrestins.

36. The method according to claim 35 wherein the protein is a phosphatase.

37. The method according to claim 36 wherein the phosphatase is SHP-2.

38. A method for identifying a compound capable of associating with a protein, wherein said protein has a natural ligand comprising at least one mechanistically significant phosphate group, said method comprising the steps of:

a.) selecting a first compound comprising a sulfhydantoin moiety or a reverse sulfhydantoin moiety; and

b.) optionally modifying said first compound to optimize at least one additional structural feature for association with said protein.

39. The method according to claim 38 wherein said optimization comprises optimizing structure-activity relationships.

40. The method according to claim 39 wherein said optimization comprises molecular modeling.

41. The method according to claim 38 wherein said protein is an enzyme.

42. The method according to claim 41 wherein said enzyme is a binding domain for the natural ligand.

43. The method according to claim 42 wherein said binding domain is a receptor for the natural ligand.

44. The method according to claim 43 wherein said receptor comprises a binding pocket.

45. The method according to claim 38 wherein said natural ligand is a substrate of the protein.

46. The method according to claim 38 wherein said natural ligand is a second protein.

47. The method according to claim 38 wherein said natural ligand is an agonist of the protein.

48. The method according to claim 38 wherein said natural ligand is an antagonist of the protein.

49. The method according to claim 38 wherein said compound is an inhibitor of the protein.

50. The method according to claim 38 wherein the protein is a phosphatase.

51. The method according to claim 50 wherein the compound is a phosphatase inhibitor.

52. The method according to claim 50 wherein the phosphatase is SHP-2.

53. The method according to claim 52 wherein the compound is an SHP-2 inhibitor.

54. A method for producing a compound capable of associating with a protein, wherein said protein has a natural ligand comprising at least one mechanistically significant phosphate group, said method comprising the step of replacing said phosphate group in said natural ligand with a sulfhydantoin moiety or a reverse sulfhydantoin moiety to produce said compound.

55. The method according to claim 54 wherein said protein is an enzyme.

56. The method according to claim 55 wherein said enzyme is a binding domain for the natural ligand.

57. The method according to claim 56 wherein said binding domain is a receptor for the natural ligand.

58. The method according to claim 57 wherein said receptor comprises a binding pocket.

59. The method according to claim 54 wherein said natural ligand is a substrate of the protein.

60. The method according to claim 54 wherein said natural ligand is a second protein.

61. The method according to claim 54 wherein said natural ligand is an agonist of the protein.

62. The method according to claim 54 wherein said natural ligand is an antagonist of the protein.

63. The method according to claim 54 wherein the compound is an inhibitor of the protein.

64. The method according to claim 54 wherein the protein is a phosphatase.

65. The method according to claim 64 wherein the compound is a phosphatase inhibitor.

66. The method according to claim 64 wherein the phosphatase is SHP-2.

67. The method according to claim 66 wherein the compound is an SHP-2 inhibitor.

68. A method of treating or preventing a disease selected from autoimmune diseases, proliferative

diseases, angiogenic disorders, and cancers in a patient comprising the step of administering to said patient a composition according to claim 10.

69. The method according to claim 68 wherein said method is used to treat or prevent an autoimmune disease selected from glomerulonephritis, rheumatoid arthritis, systemic lupus erythematosus, scleroderma, chronic thyroiditis, Graves' disease, autoimmune gastritis, diabetes, autoimmune hemolytic anemia, autoimmune neutropenia, thrombocytopenia, atopic dermatitis, chronic active hepatitis, myasthenia gravis, multiple sclerosis, inflammatory bowel disease, ulcerative colitis, Crohn's disease, psoriasis, or graft vs. host disease.

70. The method according to claim 68 wherein said method is used to treat or prevent a proliferative disease selected from acute myelogenous leukemia, chronic myelogenous leukemia, metastatic melanoma, Kaposi's sarcoma, multiple myeloma, and HTLV-1-mediated tumorigenesis.

71. The method according to claim 68 wherein said method is used to treat or prevent an angiogenic disorder selected from solid tumors, ocular neovasculization, and infantile haemangiomas.

72. The method according to claim 68 wherein said method is used to treat or prevent a cancer selected from colon, breast, stomach, and ovarian cancer.

73. The method according to claim 68 further comprising the step of administering to said patient an additional therapeutic agent.

74. The method according to claim 73 wherein said additional therapeutic agent is selected from chemotherapeutic agents, anti-proliferative agents, and anti-inflammatory agents.